

NIDA Director's Report to the NIH Collaborative Research on Addiction (CRAN) Council

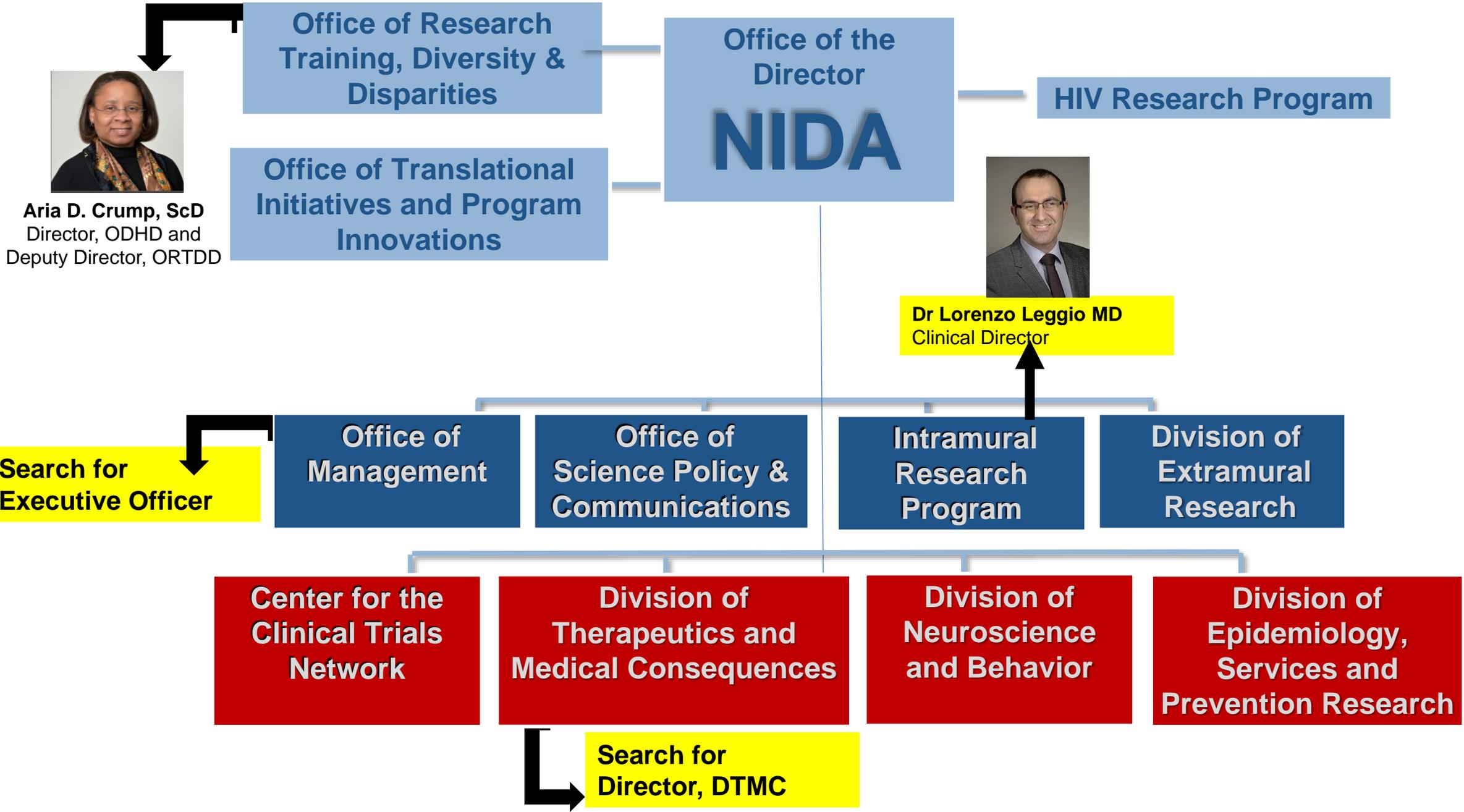
Nora D. Volkow, M.D.

Director

National Institute on Drug Abuse

National Institutes of Health

May 10, 2023



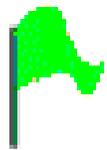
Aria D. Crump, ScD
 Director, ODHD and
 Deputy Director, ORTDD



Dr Lorenzo Leggio MD
 Clinical Director

2022 Monitoring the Future Study

Key Findings and Concerns to Watch

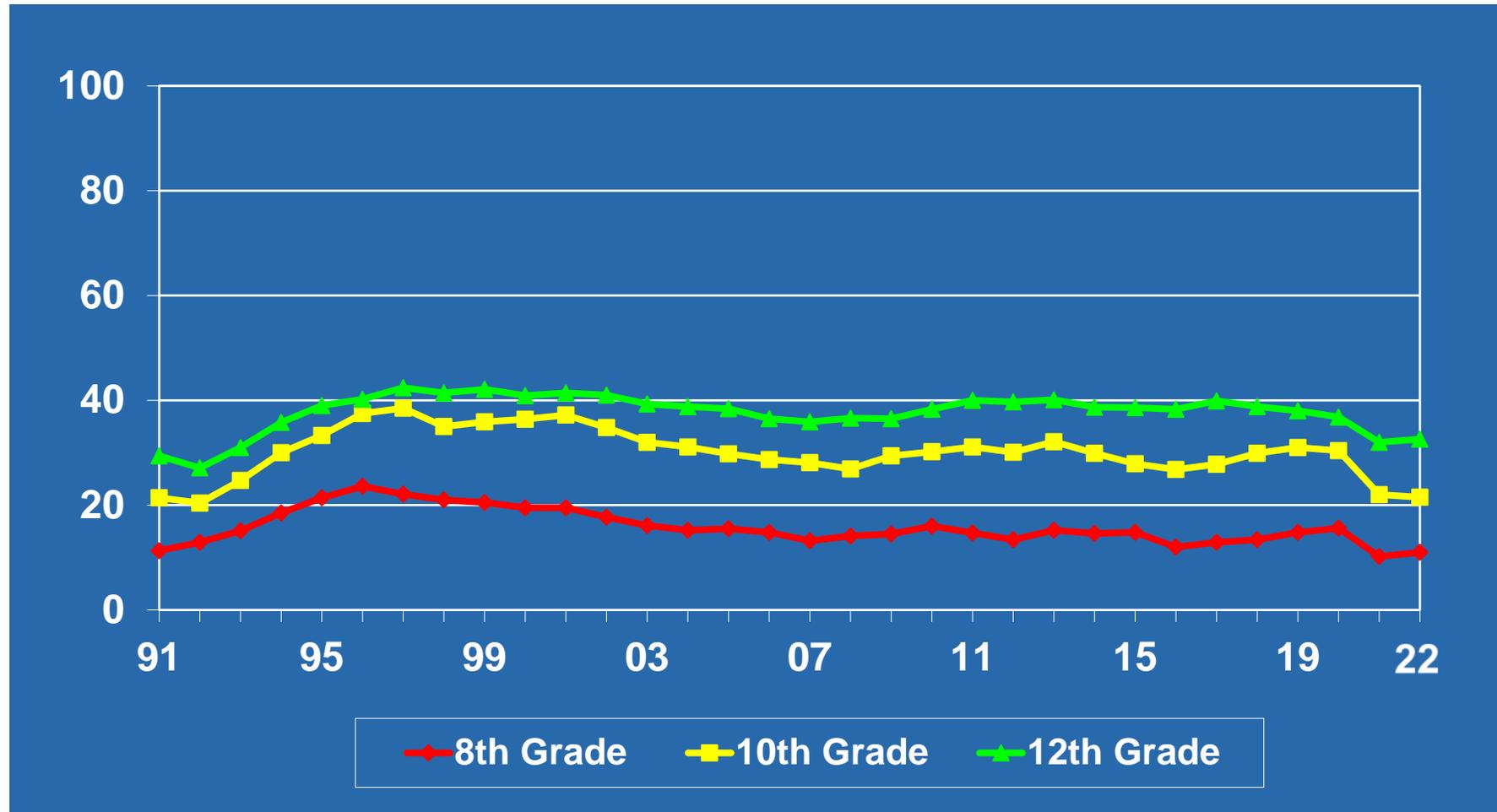


- **Most prevalences remained at or below pre-pandemic levels of use**



- **Few rebounds (notable one **alcohol 12th graders**) from last year's unprecedented number of decreases in drug use among youth**
- **How will the decreases impact outcomes longer term?**

Percent of Students Reporting Any Illicit Drug Use in Past Year, by Grade



2022 Monitoring the Future Study

Prevalence of Past Year Drug Use Among 12th graders

Drug	Prev.	Drug	Prev.
Alcohol	51.9	LSD	2.5
Vaping, Any	32.1	Sedative/Tranquilizers*	2.5
Marijuana/Hashish	30.7	Snus	2.4
Vaping MJ	20.6	Cough Medicine*	2.4
Small Cigars	5.6	OxyContin*	1.9
Hallucinogens	4.4	Inhalants	1.8
Hall other than LSD	3.4	Narcotics o/t Heroin*	1.7
Adderall*	3.4	Cocaine (any form)	1.5
Hookah	3.3	MDMA (Ecstasy)	1.4
Synthetic Cannabinoids	3.2	Vicodin*	1.3
Amphetamines*	2.8	Steroids	1.3

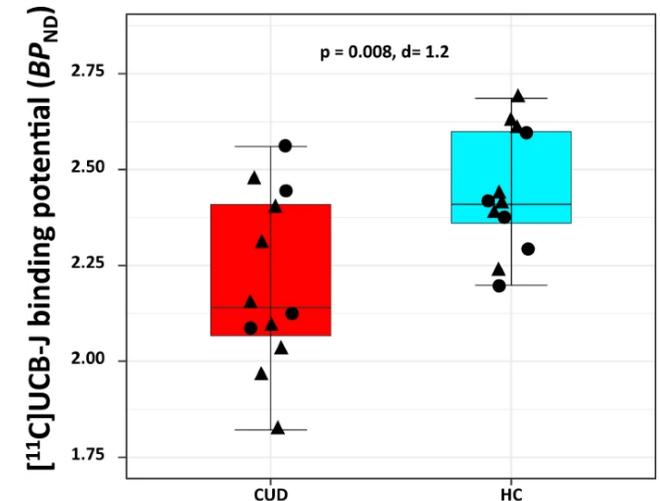
* Nonmedical use

Categories not mutually exclusive

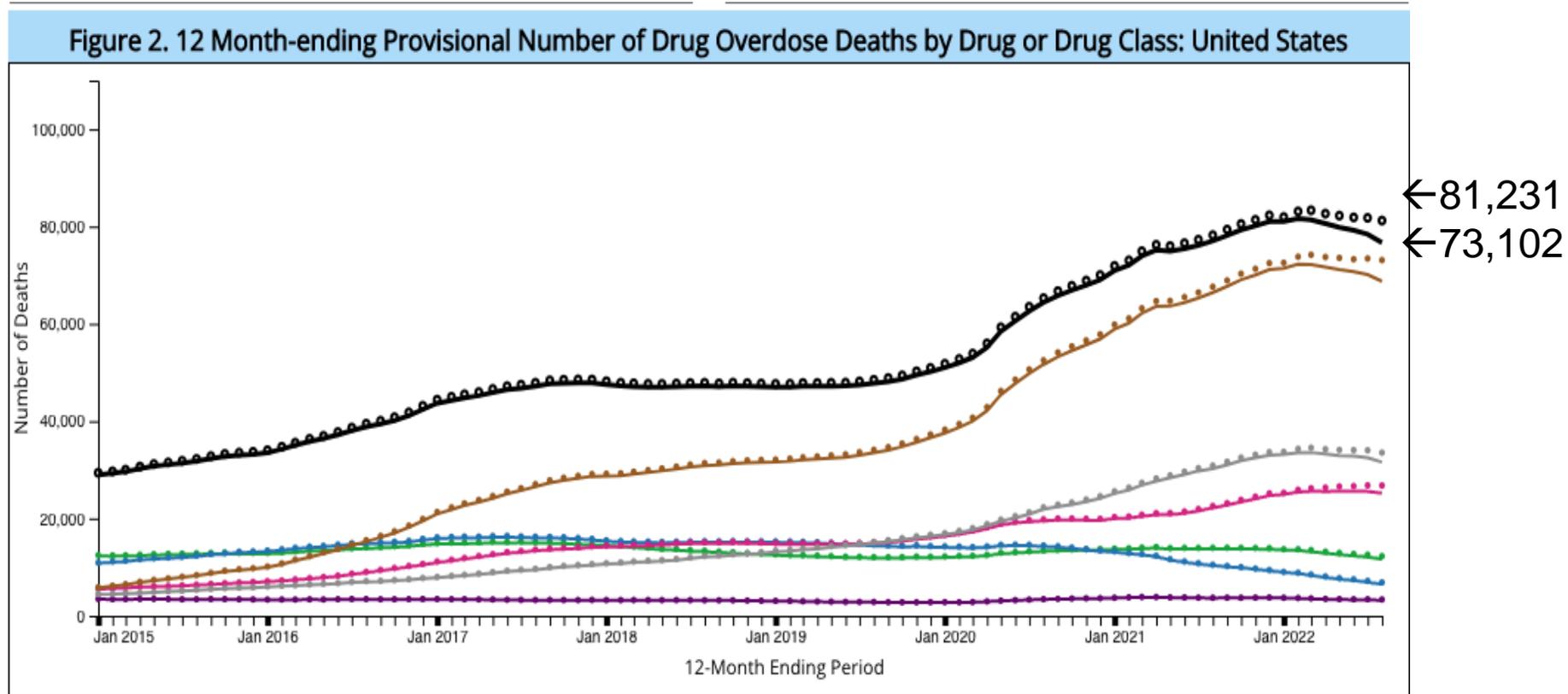
CANNABIS RESEARCH PRIORITIES

- Cannabis (THC, CBD, others) actions at molecular, epigenetic, cellular, neurocircuitry and behavioral levels.
- Patterns of cannabis consumption and polysubstance use
- Investigation of risk factors for cannabis use and CUD (genetic, developmental, SDH).
- Consequences of cannabis use in brain, health and behaviors across the lifespan including neurodevelopment (fetal and childhood) and neurodegeneration.
- **Prevention and therapeutic Interventions for CUD**
- Impact of different policies on patterns of cannabis consumption and its consequences
- Medical cannabis potential in management of SUD, HIV or pain.

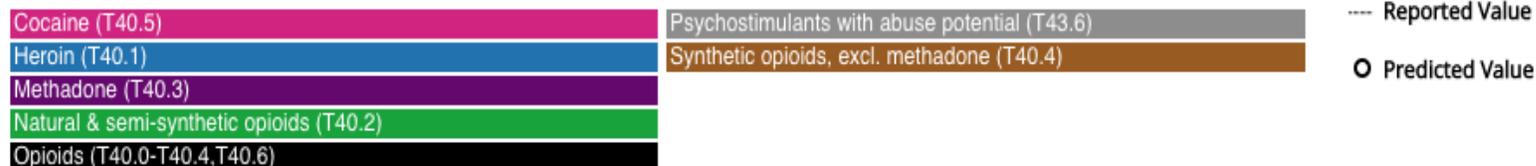
Hippocampal synaptic density (PET [¹¹C]UCB-J BP_{ND})



Synthetics Are Now Linked to Almost 90% of Opioid Overdose Deaths



Legend for Drug or Drug Class



counts.

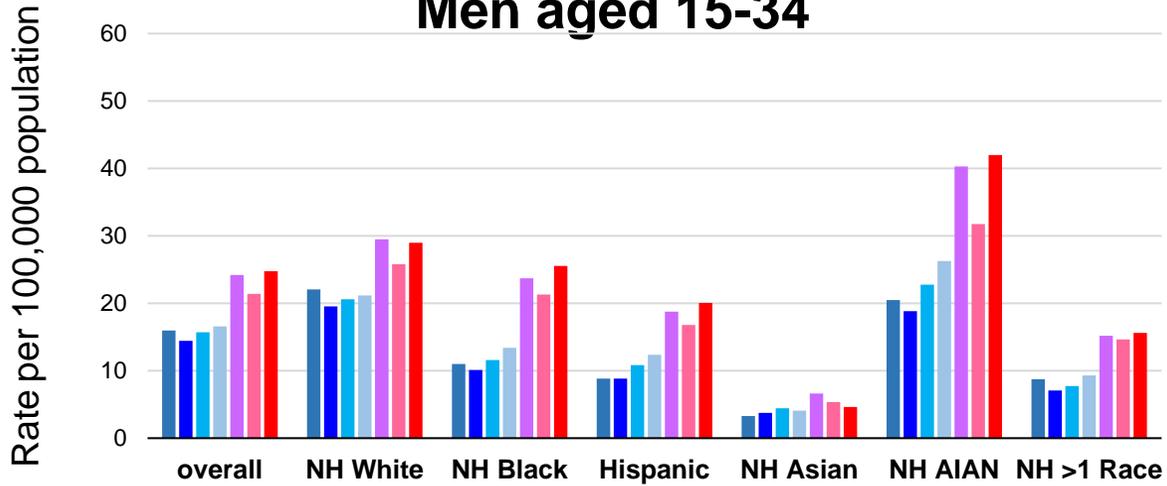
National Center for Health Statistics. 2022

Why are FENTANYL and analogues so dangerous?

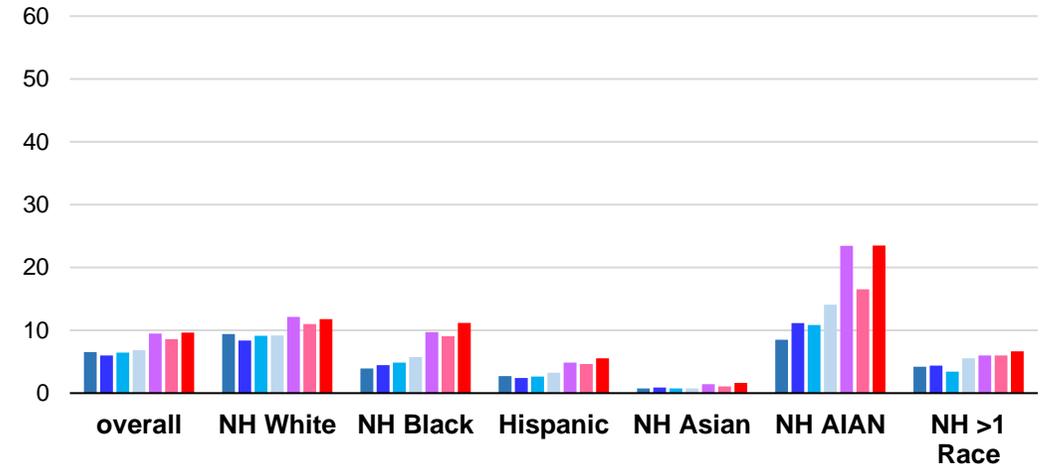
- Potency: fentanyl is ~50x more potent (mg/kg basis) than heroin; 2mg can be lethal
- Lack of pharmaceutical standards; fentanyl doses used to lace other drugs vary (i.e., for counterfeit pills DEA reports that doses can range from .02 to 5.1 mg)
- Fentanyls are more lipophilic than heroin; rapid brain penetration → faster onset [reduced time for naloxone rescue]
- **Overdose reversals from fentanyl require higher and multiple naloxone doses**
- **Physical dependence from fentanyl is stronger than for heroin making treatment initiation with medications for OUD more challenging.**

Overdoses Before and During the COVID-19 Pandemic

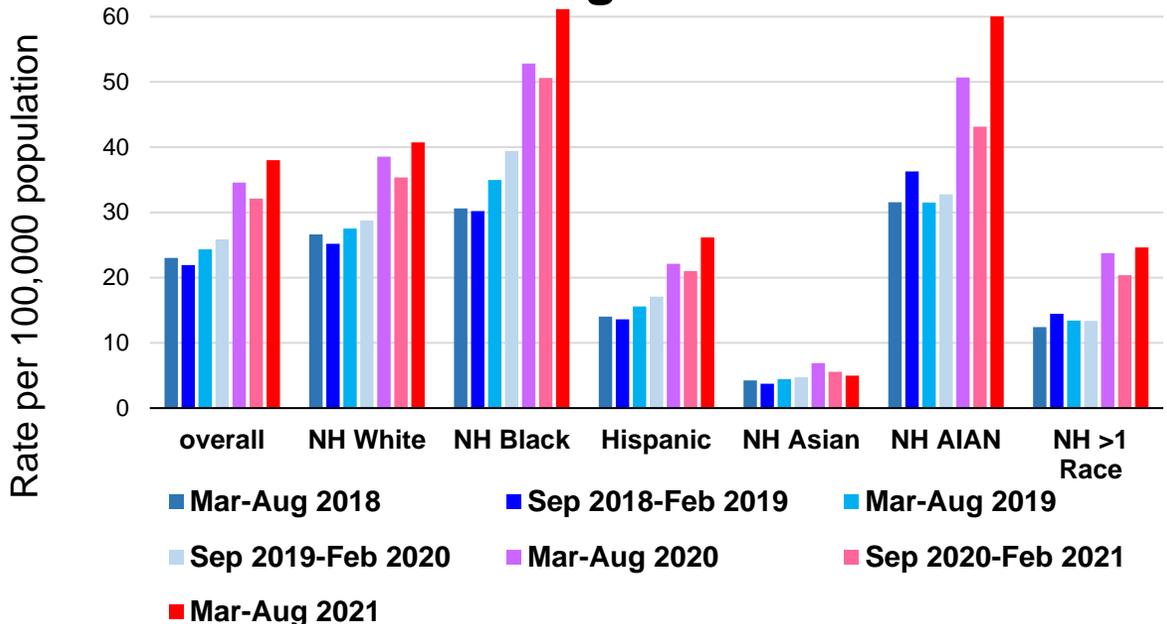
Men aged 15-34



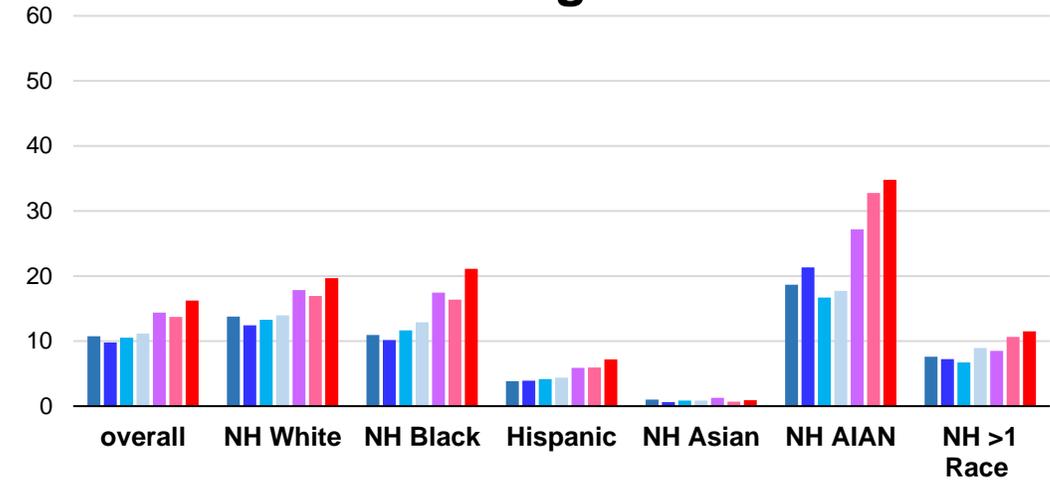
Women aged 15-34



Men aged 35-64

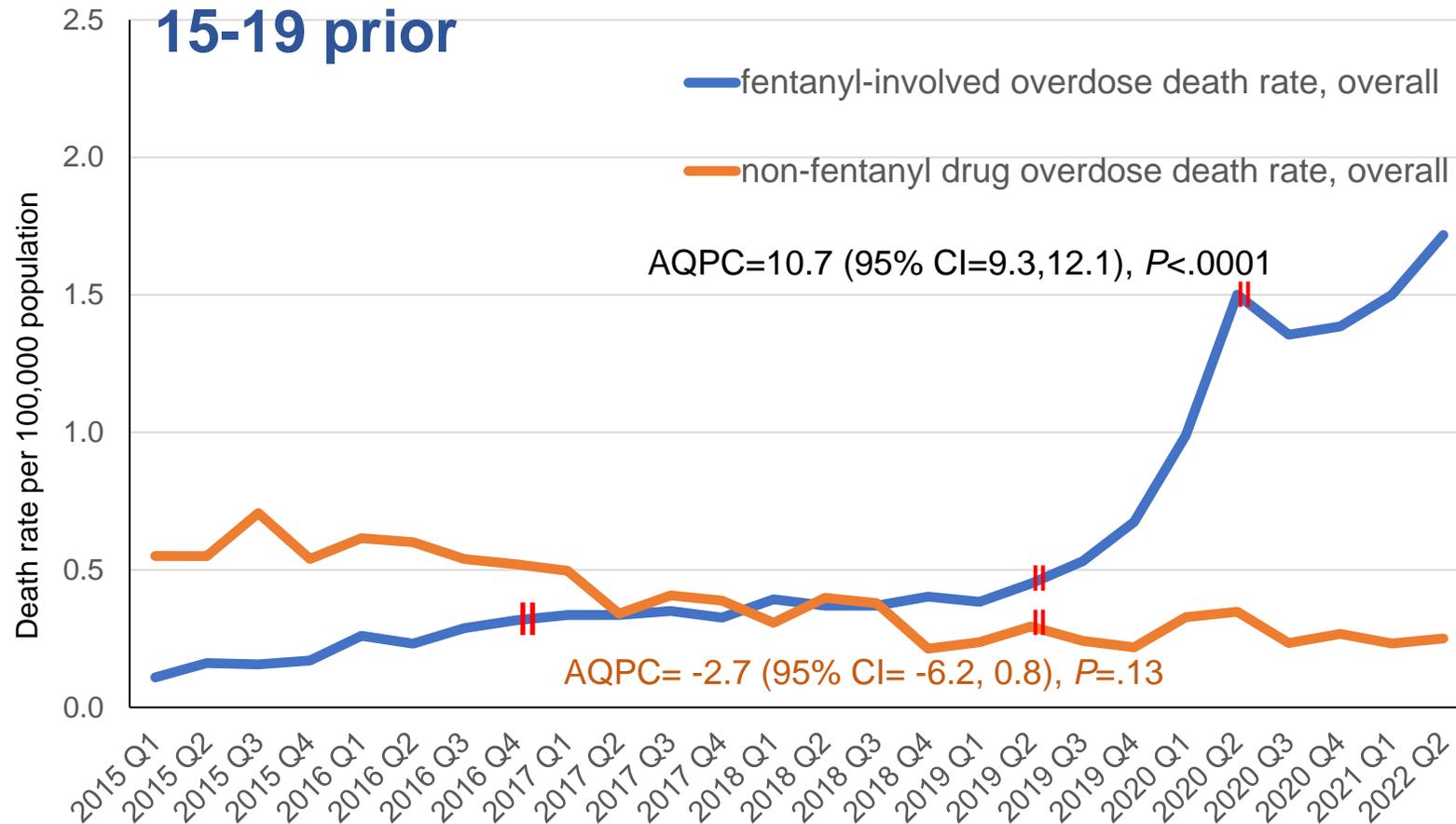


Women aged 35-64



NH: non-Hispanic. AIAN: American Indian/Alaska Native. March-August 2020: COVID-19 pandemic.

Fentanyl-involved and non-fentanyl overdose death rates in US youth aged 15-19 prior

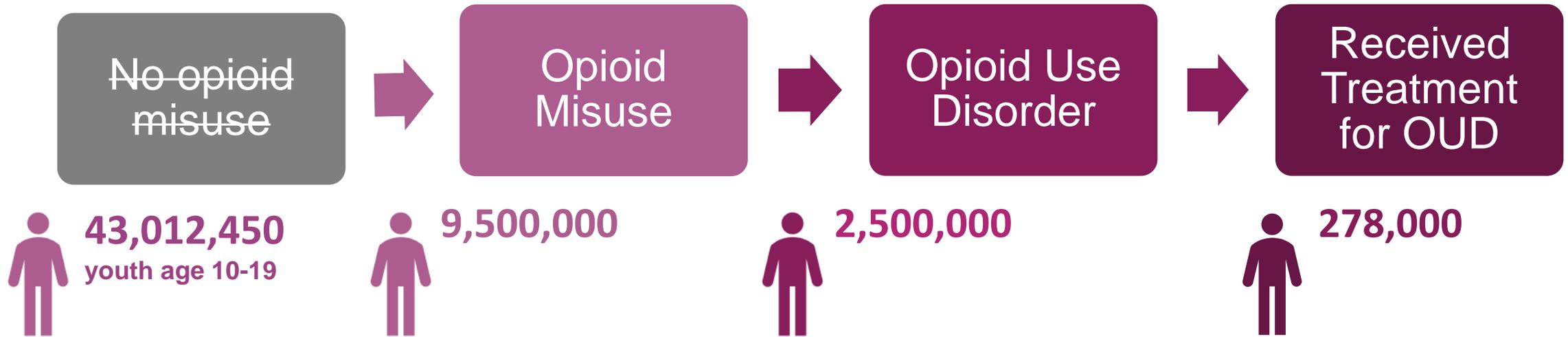


National Vital Statistics System multiple-cause-of-death 2015-2020 final and 2021 provisional data U.S. census monthly data. **||**: Joinpoints indicate significant changes in nonlinear trends using Bayesian Information Criterion. AQPC=average quarter percentage change during 2015 Q1-2022 Q2. ICD-10 cause of death code: synthetic opioids other than methadone (T40.4, primarily fentanyl and analogs).

Research Needs

- Implementation research of screening interventions for substance misuse and SUD in teenagers
- Research on interventions to prevent drug misuse in teenagers and in the transition into young adulthood
- Treatment of SUD in teenagers including mild, moderate and severe OUD

SUD/ODU Prevention Cascade in US



Data Source: National Survey on Drug Use and Health

- **Social determinants of health**
- Interventions informed by scientific and technological advances
- Implementation, scale-up and sustainment of prevention services

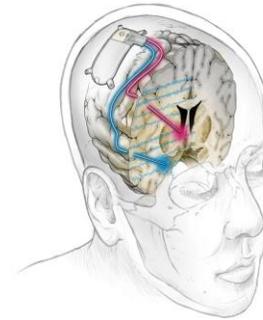
**INFRASTRUCTURE NEEDED TO DEPLOY
AND SUSTAIN PREVENTION**

Treatment Research Gaps In OUD and OD

Treatment

- Need for extended-release MOUD. Greatest need is for methadone
- Development of clinically meaningful alternative end points for clinical trials, including patient-reported outcomes
- Medications with target other than MOR (e.g., other opioid receptors, D3R, mGluR, CRF receptors)
- Repurpose medications (ie orexin receptor antagonist such as suvorexant, glucagon-like peptide agonists)
- Immunotherapies: vaccines and monoclonal AB
- Neuromodulation (TMS, tDCS, LIFU, DBS, peripheral nerve stimulation)
- Fast, high-affinity MOR antagonists with longer duration
- Respiratory stimulating drugs

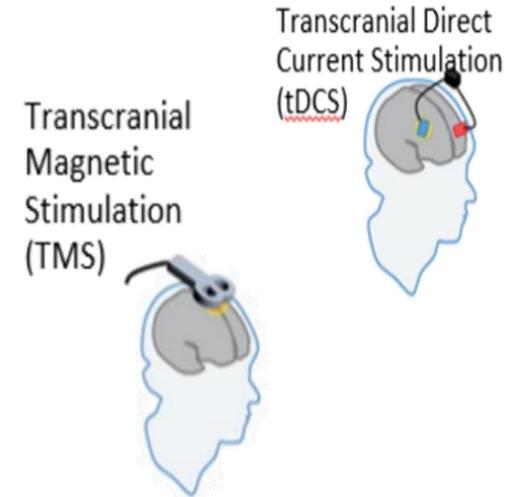
Invasive Neuromodulation Techniques



Deep Brain Stimulation

High Intensity Ultrasound (ablative)

Non Invasive Neuromodulation Techniques



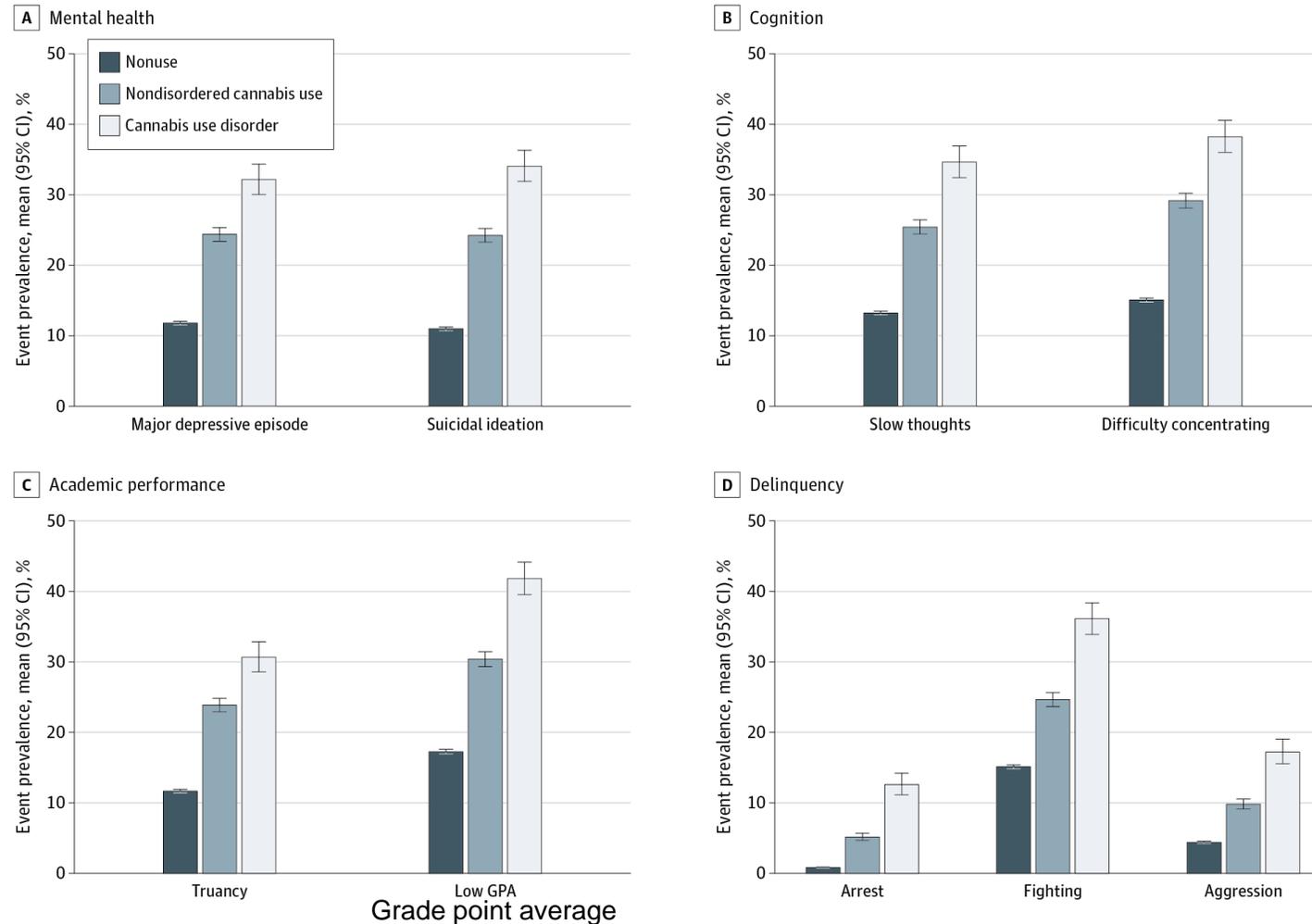
Low Intensity Ultrasound

THANK YOU!

Adverse Adolescent Psychosocial Events Among Nonuse, Non-disordered Cannabis Use, and Cannabis Use Disorder

NSDUH Data 2015-2019

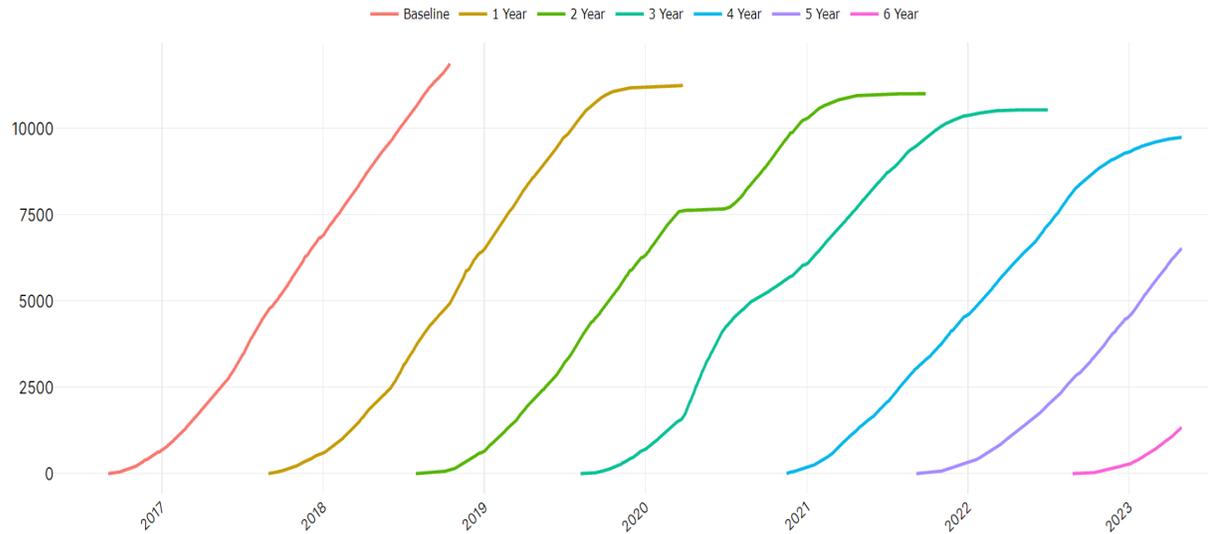
Sultan et al., JAMA Netw Open. 2023;6(5):e2311294.



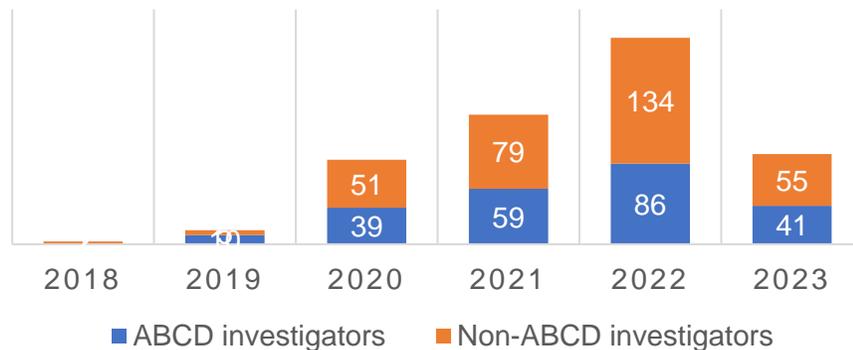
NDCU and CUD were significantly associated with adverse psychosocial events in a stepwise gradient manner

Adolescent Brain Cognitive Development Study

97.1% Percent Retained



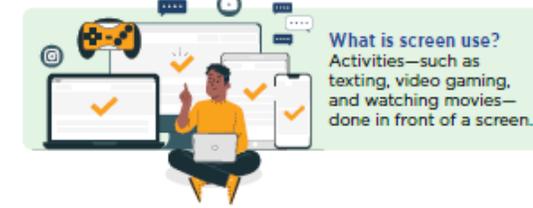
PUBLICATIONS N=562



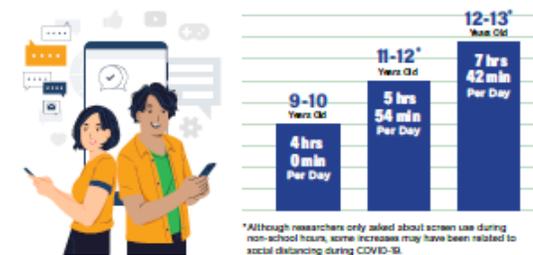
Screen use by Teenagers



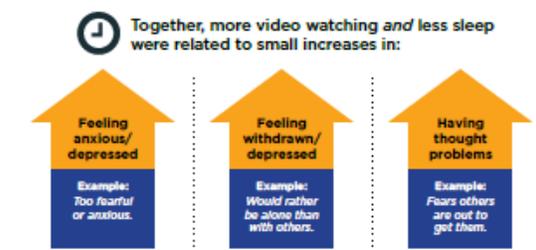
Research using data from the ABCD Study[®], the largest long-term study of brain development and child health in the United States, has shown both positive and negative associations of screen use for preteens.



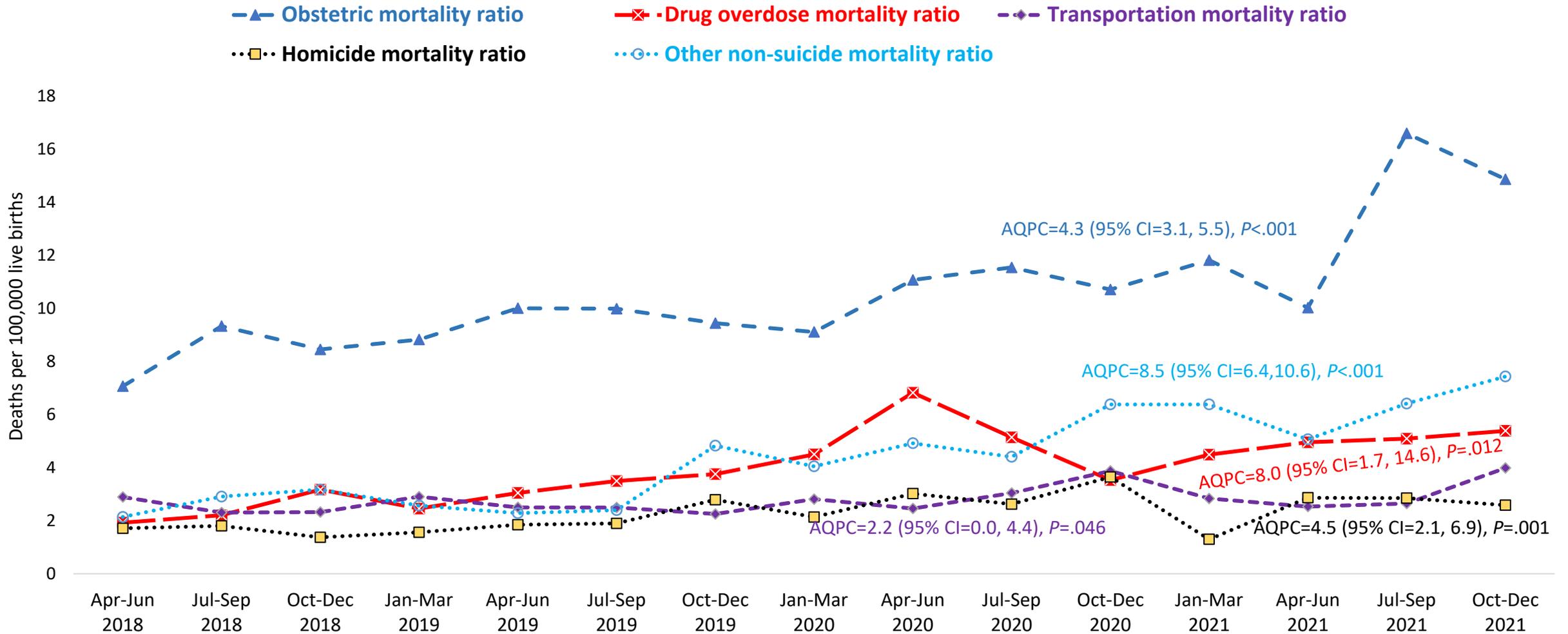
Youth use screens more as they get older



Every additional hour spent watching videos meant less sleep



Trends in mortality ratios by cause among pregnant women in 50 states and DC



Data sources: National Vital Statistics System: 2018-2021 final mortality data and 2018-2021 final birth data. Mortality ratio=deaths among pregnant women by causes/live births*100,000; AQPC=average quarter percentage change. Intentional overdose deaths were included in “deaths by suicide”. Assault deaths by drug overdose were included in “homicide deaths”. “Drug overdose” deaths included overdose deaths with unintentional or undetermined intent only. Other non-suicide deaths included deaths caused by COVID-19 infection, myocardial infarction, cancer, etc. The COVID-19 pandemic began in March 2020 and ICD-10 code U07.1 was effective in April 2020. Trends in the suicide mortality ratio among pregnant women are not presented because most quarterly deaths are under 10.